REMARKS

Claims 1-9 and 25-29 are pending. Claims 10-24 were previously canceled. Claims 7-9 and 27 have been withdrawn by the Examiner as drawn to nonelected species. Applicant respectfully reminds the Examiner that upon finding allowable subject matter, applicant is entitled to have the withdrawn claims rejoined and considered in this application as provided by 37 C.F.R. 1.141. *See* M.P.E.P. § 809.02(a). Claims 1-6, 25, 26, 28, and 29 are under consideration.

Claim 1 has been amended to replace the language "G1 or G0" with "G1 and G0" and to correct a minor typographical error. Support for that amendment is found in the specification, for example, at page 14, line 6-13. Claim 28 has been amended to correct a minor typographical error. No new matter has been added.

Provisional Rejection of Claims 1-6, 25, 26, 28, and 29

The Examiner provisionally rejected claims 1-6, 25, 26, 28, and 29 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-9, 20, 35, 37, 39, 41, and 43 of copending U.S. Application No. 10/744,844. Action at page 1, item no. 5. No action is believed required by the applicant at this time as the alleged conflicting claims have not in fact been patented.

Rejection of Claims 1-6, 25, 26, 28, and 29 Under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 1-6, 25, 26, 28, and 29 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Action at page 2, item no. 7. The Examiner alleges that "[t]here is no support in the specification as

originally filed for the recitation of 'G1 or G0 oligosaccharide does not exceed 10% by weight of the preparation.'" *Id.* Applicant respectfully traverses the rejection.

Solely to expedite prosecution, and without acquiescing to the Examiner's contentions, applicant has amended claim 1 to include the language "G1 and G0 oligosaccharide does not exceed 10% by weight of the preparation." The Examiner has acknowledged that "the specification discloses support for the limitation 'G1 **and** G0 oligosaccharide does not exceed 10% by weight of the preparation.'" *Id.* (emphasis in original). Accordingly, the rejection with respect to claim 1 is moot. Claims 2-6, 25, 26, 28 and 29 ultimately depend from claim 1 and thus also include the language "G1 and G0." Therefore, the rejection is moot with respect to those claims. Accordingly, applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-6, 25, 26, 28, and 29 under § 112, first paragraph, as allegedly failing to comply with the written description requirement.

Withdrawal of the Rejection of Claims 1-5, 25, and 28 Under 35 U.S.C. § 102(b)

Applicant acknowledges, with appreciation, the Examiner's withdrawal of the rejection of claims 1-5, 25, and 28 under 35 U.S.C. § 102(b) as allegedly being anticipated by Kumpel et al., Human Antib. Hybridomas 5:143-151 (1994) ("Kumpel"). Action at page 3, item no. 9.

Rejection of Claims 1-6, 25, 26, 28, and 29 Under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-6, 25, 26, 28, and 29 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kumpel in view of U.S. Patent No. 5,834,251 issued to Maras et al. ("Maras"). Action at page 3, item no. 11.

The Examiner acknowledges that "Kumpel et al. do not teach that the antibodies are of the degree of purity recited in the claims or the articles of manufacture of claim 29." *Id.* The Examiner, however, contends that

> Maras et al. teach that B-1,4 Galactosyltransferase can be used to modify the oligosaccharide profile on a glycoprotein (see columns 12 and 16). Kumpel et al. teach that said enzyme is involved in the production of G2 oligosaccharides (see abstract). A routineer would have used the method of Maras et al. to produce a more highly purified version of the G2 oligosaccharide containing antibody to further characterize the role of said oligosaccharides in effector function and to produce an antibody with even greater effector function.

Id. at pages 3-4.

The Examiner alleges that

> [i]t would have been prima facie obvious to one of ordinary skill in the art to have created the claimed invention because Kumpel et al. teach that antibodies with substantially all G2 oligosaccharide have increased lysis of target cells in comparison to the same antibody which is produced in a manner that results in low levels of G2 and Maras et al. teach that B-1,4 Galactosyltransferase can be used to modify the oligosaccharide profile on a glycoprotein (eg. to produce highly pure G2 oligosaccharide glycoproteins).

Id. at page 4.

Applicant respectfully traverses the rejection. The Examiner has failed to establish a *prima facie* case of obviousness.

As provided in the M.P.E.P. at § 2141, and in the "Examination Guidelines for Determining Obviousness in Light of the Supreme Court's KSR v. Teleflex Decision," 72 FR 57526-57535 published on October 10, 2007 ("Guidelines"), it is Office policy to follow *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) in the consideration and determination of obviousness under § 103. As stated in the M.P.E.P, *Graham* provides

> four factual inquiries . . . as a background for determining obviousness [a]s follows:
>
> (A) Determining the scope and contents of the prior art;
> (B) Ascertaining the differences between the prior art and the claims in issue;
> (C) Resolving the level of ordinary skill in the pertinent art; and
> (D) Evaluating evidence of secondary considerations.

M.P.E.P. at § 2141 at page 2100-116. In addition, the Guidelines instruct that "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness," and provides seven possible rationales. *Id.* at 57529.

For a rationale based on "some teaching, suggestion, or motivation in the prior art," the Guidelines provide that

> Office personnel must resolve the *Graham* factual inquiries. Office personnel must then articulate the following:
>
> (1) a finding that there was some teaching, suggestion, or motivation . . . to modify the reference or to combine reference teachings;
>
> (2) a finding that there was reasonable expectation of success; and
>
> (3) whatever additional findings based the *Graham* factual inquiries may be necessary . . . to explain a conclusion of obviousness.
>
> The rationale to support a conclusion that the claim would have been obvious is that 'a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success.'

Guidelines at 57534. Importantly, the Guidelines further instruct that "[i]f **any** of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art." *Id.* (emphasis added).

Specifically, the Examiner has <u>not</u> provided a finding of "some teaching, suggestion, or motivation . . . to modify the reference or to combine reference teachings" to achieve the claimed invention. With respect to Kumpel, while the document does discuss at page 149 certain "hypergalactosylated" antibodies that "promoted greater FcγRI- and FcγRIII-mediated lysis of erythrocytes in ADCC assays than the anti-D with a lower galactose content," it also discusses different results with certain other antibodies having differences in sialylation. For example, Kumpel discusses that two antibodies (JAC10 LD and 2B6 LD) with similar galactosylation

levels, but different sialylation levels, had different target cell lysis activity. Kumpel at page 149, right column, second full paragraph. Specifically, Kumpel notes that "[o]ne MAb, JAC10, was over 10-fold less active than two other IgG1 MAbs, 2B6 and BRAD-5, at mediating lysis of erythrocytes by FcγRIII+ K cells; **differences in sialylation** may have contributed to this heterogeneity." Kumpel, abstract (emphasis added). In addition, Kumpel discusses that "[a]ssays of the comparative functional activity of the IgG1 subclass MAbs showed that while 2B6 and BRAD-5 were active, JAC10 was very poor at mediating FcγRIII-mediate lysis." Kumpel at page 149, right column. Kumpel further states that "[t]he relatively high degree of sialylation of JAC10 may have contributed to its poor FcγRIII-mediated activity." Therefore, because Kumpel discusses not only effects of oligosaccharide galactosylation on target cell lysis mediated by antibodies, but also effects of sialylation on target cell lysis, one skilled in the art would not have been motivated "to produce a more highly purified version of the G2 oligosaccharide containing antibody" as proposed by the Examiner. It would not have been predictable that a "glycoprotein having an immunoglobulin CH2 domain said CH2 domain having at least one N-linked oligosaccharide wherein substantially all of the oligosaccharide is a G2 oligosaccharide and wherein the amount of said glycoprotein containing G1 and G0 oligosaccharide does not exceed 10% by weight of the preparation," according to claim 1 would have improved functional activity, for example, in antibody-dependent cellular toxicity and complement mediated cell lysis.

Maras fails to cure the deficiencies of Kumpel. Maras discusses "the development of methods of preparing hybrid and complex glycosylation patterns, similar to those found in mammalian hosts." Maras at col. 2, lines 40-43. Maras further discusses that "the glycosylation pattern of a desired protein (glycoprotein) is sequentially modified by reaction with N-

actylglucosaminyl-transferase I . . . , galactosyltransferase and sialyltransferase, so as to produce a protein having a hybrid-type glycosylation pattern with terminal sialic acid(s) similar to that of mammalian cells. *See, e.g.*, Maras at col. 2, lines 44-50. Nowhere does Maras discuss "a glycoprotein preparation . . . wherein substantially all of the oligosaccharide is a G2 oligosaccharide and wherein the amount of said glycoprotein containing G1 and G0 oligosaccharide does not exceed 10% by weight of the preparation," according to the claims. Accordingly, one skilled in the art at the time the application was filed would have had no reason to use "the method of Maras et al. to produce a more highly purified version of the G2 oligosaccharide containing antibody," as the Examiner contends.

Therefore, the Examiner has not provided a finding of "some teaching, suggestion, or motivation . . . to modify the reference or to combine reference teachings" and thus, has not established a *prima facie* case of obviousness. Accordingly, claim 1 would not have been obvious in view of Kumpel and/or Maras, nor would any of dependent claims 2-6, 25, 26, 28, and 29 have been obvious. Therefore, applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-6, 25, 26, 28, and 29 under § 103(a) as allegedly being unpatentable over Kumpel in view of Maras.

Because the Examiner fails to establish that claims 1-6, 25, 26, 28, and 29 would have been obvious for at least the reasons discussed above, applicant need not address the Examiner's contentions concerning other elements of those claims. By not addressing those contentions, applicant in no way acquiesces to those contentions.

CONCLUSION

Applicant respectfully asserts that the claims are in condition for allowance and requests the timely issuance of a Notice of Allowance. Should the Examiner believe that a telephone

interview would expedite the prosecution of this application, applicant invites the Examiner to call the undersigned at the telephone number indicated below.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 07-0630.

Respectfully submitted,

GENENTECH, INC.

Dated: March 21, 2008

By: _____

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